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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,637	04/13/2001	Yoshikatsu Kodama	011900-309	3072
7590 02/09/2004				
Platon N. Mandros BURNS, DOANE, SWECKER & MATHIS, L.L.P. P.O. Box 1404 Alexandria, VA 22313-1404			EXAMINER KAM, CHIH MIN	
			ART UNIT 1653	PAPER NUMBER

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/833,637

Applicant(s)

KODAMA ET AL.

Examiner

Chih-Min Kam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-15 and 22-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 27-30 is/are allowed.
- 6) ☒ Claim(s) 12-15, 22-26 and 31-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. The Request for Continued Examination (RCE) filed August 4, 2003 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

Status of the Claims

2. Claims 12-15 and 22-34 are pending.

Applicants' amendment filed on December 12, 2003 is acknowledged. Applicants' response has been fully considered. Claim 22-26 have been amended, claims 16-21 have been cancelled, and new claims 31-34 have been added. Upon consideration, claims 22-26, which are directed to a method of inhibiting *Helicobacter pylori* colonization or a method for preventing or treating a disease caused by or associated with *Helicobacter pylori* using the glycoprotein, are included for examination. Therefore, claims 12-15 and 22-34 are examined. A proposed Examiner's amendment has been faxed to applicant on January 20, 2004, but the proposed amendment has not been accepted.

Objection Withdrawn

3. The previous objection of claims 17-21, is withdrawn in view of applicants' cancellation of the claim in the amendment filed December 12, 2003.

Rejection Withdrawn

Claim Rejections - 35 USC § 102

4. The previous rejection of claims 16 and 22-26, under 35 U.S.C. 102(b) as being anticipated by Peterson *et al.* (U. S. Patent 5,505,955), is withdrawn in view of applicants' amendment to the claim, applicant's cancellation of the claim, and applicants' response at pages 8-11 in the amendment filed December 12, 2003.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 12-15, 23, 24 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting *Helicobacter pylori* (*H. pylori*) colonization, or treating a specific gastrointestinal disease such as peptic ulcers caused by *H. pylori* in mammals, comprising orally administering a glycoprotein which specifically binds to urease of *H. pylori*, or a glycoprotein and an inhibitor of gastric acid secretion, wherein the glycoprotein is isolated and purified from a glycoprotein-containing substance from whey of bovine milk or albumen of chicken eggs using a method of specific adsorption to the *H. pylori* urease; a pharmaceutical composition for treating the specific gastrointestinal disease caused by *H. pylori*, comprising the glycoprotein, or the glycoprotein and an inhibitor of gastric acid secretion; or a food that treats the specific gastrointestinal disease caused by *H. pylori*, comprising the glycoprotein, does not reasonably provide enablement for a method of inhibiting *H. pylori* colonization, or treating or preventing (not even occurs at the first time) a disease caused by or associated with *H. pylori* in mammals, comprising orally administering a glycoprotein which specifically binds to urease of *H. pylori*, or a glycoprotein and an inhibitor of gastric acid secretion, wherein the glycoprotein is isolated and purified from a glycoprotein-containing substance using a method of specific adsorption to the *H. pylori* urease; a pharmaceutical composition for preventing or treating a disease caused by or associated with *H. pylori*, comprising the glycoprotein, or the glycoprotein and an inhibitor of gastric acid secretion;

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or a food that prevents or treats a disease caused by or associated with *H. pylori*, comprising the glycoprotein, where the source of the glycoprotein and the disease are not defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 12-15, 23, 24 and 26 are directed to a method of inhibiting *H. pylori* colonization (claims 12 and 13), or treating or preventing a disease caused by or associated with *H. pylori* (claims 14 and 15) in mammals, comprising orally administering a glycoprotein which specifically binds to urease of *H. pylori*, or a glycoprotein and an inhibitor of gastric acid secretion, wherein the glycoprotein is isolated and purified from a glycoprotein-containing substance using a method of specific adsorption to the *H. pylori* urease; a pharmaceutical composition for preventing or treating a disease caused by or associated with *H. pylori*, comprising the glycoprotein (claim 23), or the glycoprotein and an inhibitor of gastric acid secretion (claim 26); or a food that prevents or treats a disease caused by or associated with *H. pylori*, comprising the glycoprotein (claim 24). The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the instant invention is to provide an effective and safe inhibitor of *H. pylori* colonization which is associated with the occurrence of peptic ulcers, and to provide a medicament and food useful for treating or preventing peptic ulcers, where the inhibitor is a glycoprotein is obtained from whey of bovine milk or albumen of chicken eggs (pages 3-4). There are no indicia that the present application enables the full scope in view of the method of inhibiting *H. pylori* colonization, or treating or preventing a disease caused by or associated with *H. pylori* using a glycoprotein which

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specifically binds to urease of *H. pylori* as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the identity of the glycoprotein from other sources, the treating conditions for treating or preventing various *H. pylori*-associated diseases, and the effects of the glycoprotein in the treatment, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The in vitro studies indicate urease adherence to porcine gastric mucin was inhibited dose-dependently with high-molecular-weight whey protein concentrate, high-molecular-weight albumen protein concentrate, and the glycoprotein purified from each concentrate (Fig. 2 and page 19 second paragraph); and in vivo experiment indicates the glycoprotein could eliminate *H. pylori* from the stomach of *H. pylori*-colonized mice in a concentration-dependent manner, thus, it is thought the glycoprotein can inhibit the infection with *H. pylori* by binding to the urease produced by *H. pylori* and masking the urease, an adhesin, and the combination of the glycoprotein and an inhibitor of gastric acid secretion showed enhanced efficacy (Fig. 3 and

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pages 19-20). However, there are no working examples indicating the claimed methods in association with the variants, e.g., the glycoprotein from other sources, and the treating conditions for treating or preventing various *H. pylori*-associated diseases, and the effects of the glycoprotein in the treatment of various *H. pylori*-associated diseases.

(3). The state of the prior art and relative skill of those in the art:

The related art (references on page 2 of the specification) indicates the milk fat globule membrane fraction inhibits haemagglutination of *H. pylori*, and there was no correlation between expression of haemagglutination by *H. pylori* bacteria and the ability to bind gastric mucosa cells, it appears that the art does not teach or suggest a substance capable of inhibiting adherence of *H. pylori* to gastric mucosa. Thus, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on identity of the glycoprotein from other sources, the treating conditions for treating or preventing various *H. pylori*-associated diseases, and the effects of the glycoprotein in treating various *H. pylori*-associated diseases to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a method for treating or preventing a *H. pylori*-associated disease in mammals, comprising administering a glycoprotein which specifically binds to urease of *H. pylori*, or a glycoprotein and an inhibitor of gastric acid secretion. However, the specification has not described the treating conditions such as dosage for treating various *H. pylori*-associated diseases, nor has demonstrated the effect of the glycoprotein in treating or preventing various *H. pylori*-associated diseases, the invention is highly unpredictable regarding the outcome of the treatment of these diseases.

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(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of inhibiting *H. pylori* colonization, or, treating or preventing a *H. pylori*-associated diseases in mammals, comprising administering a glycoprotein which specifically binds to urease of *H. pylori*, or a glycoprotein and an inhibitor of gastric acid secretion; a pharmaceutical composition for preventing or treating a disease caused by or associated with *H. pylori*, comprising the glycoprotein or the glycoprotein and an inhibitor of gastric acid secretion; or a food that prevents or treats a disease caused by or associated with *H. pylori*, comprising the glycoprotein. The specification indicates urease adherence to porcine gastric mucin was inhibited dose-dependently with high-molecular-weight whey protein concentrate, high-molecular-weight albumen protein concentrate, and the glycoprotein purified from each concentrate (Fig. 2 and page 19 second paragraph); and the glycoprotein could eliminate *H. pylori* from the stomach of *H. pylori*-colonized mice in a concentration-dependent manner (Fig. 3 and pages 19-20), thus the adherence of *H. pylori* to gastric mucosa can be blocked effectively using a small amount of glycoprotein and diseases caused by *H. pylori* such as peptic ulcers can be suppressed effectively without the occurrence of side effects (page 26). However, there are no working examples indicating the identity of glycoprotein from other sources, or the treating conditions such as the dose for treating or preventing various *H. pylori*-associated diseases, nor demonstrating the effects of the glycoprotein, the pharmaceutical composition or the food comprising the glycoprotein in the treatment or prevention of various *H. pylori*-associated diseases. Moreover, the specification does not provide any specific guidance such as the dose, the time on the treatment of a *H. pylori*-associated disease, nor describes how to

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prevent the disease, e.g., if the disease does not occur, how to monitor it. Therefore, it is necessary to have additional guidance on the treating conditions for treating various *H. pylori*-associated diseases, and to carry out further experimentation to assess the effect of the glycoprotein in the treatment.

(6). Nature of the Invention

The scope of the claims encompass a method of inhibiting *H. pylori* colonization, or, treating or preventing a *H. pylori*-associated diseases in mammals, comprising administering a glycoprotein which specifically binds to urease of *H. pylori*; a pharmaceutical composition for preventing or treating a disease caused by or associated with *H. pylori*, comprising the glycoprotein or the glycoprotein and an inhibitor of gastric acid secretion; or a food that prevents or treats a disease caused by or associated with *H. pylori*, comprising the glycoprotein, but the specification only shows the glycoprotein isolated from a glycoprotein-containing substance from whey of bovine milk or albumen of chicken eggs and specifically bound to the *H. pylori* urease inhibits *H. pylori* colonization, it does not demonstrate the effect of the glycoprotein from various sources in treating or preventing various *H. pylori*-associated diseases. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods and variants, the outcome of treatment is unpredictable using the glycoprotein, and the teachings in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the glycoprotein in treating or preventing various *H. pylori*-associated diseases in vivo.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 14, 15, 22-26 and 31-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 14 and 15 are indefinite because the claim lacks an essential step in the method of treating or preventing a disease caused by or associated with an *H. pylori*. The omitted step is the outcome of the method. The term “preventing or treating the disease” is not the end point of the method because it does not indicate the effect of the glycoprotein administered, thus it is not clear whether the treatment is effective.

8. Claims 22-26 and 31-34 are indefinite because of the use of the term “An inhibitor of *Helicobacter pylori* colonization, consisting essentially of a glycoprotein”. The term cited renders the claim indefinite, it is not clear whether “an inhibitor” is a composition or a compound, if it is a composition consisting essentially of a glycoprotein, it should be indicated as inhibitor composition, and if it is a compound, it can only be a glycoprotein and cannot use the term “consisting essentially of a glycoprotein”. Claims 23-26 and 31-34 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

9. Claims 14, 15, 23, 24 and 26 are indefinite as to “a disease caused by or associated with *Helicobacter pylori*” or “a gastrointestinal disease caused by or associated with *Helicobacter*

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pylori", it is not clear what disease is caused by *Helicobacter pylori*, and what disease is a disease associated with *Helicobacter pylori*.

Conclusion

10. Claims 12-15, 22-26 and 31-34 are rejected. It appears claims 27-30 are free of prior art.

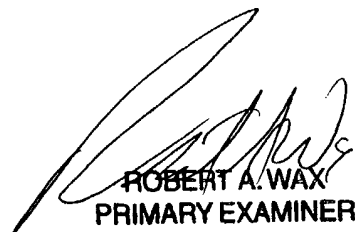
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. *CMK*
Patent Examiner

January 28, 2004


ROBERT A. WAX
PRIMARY EXAMINER